

**REMARKS**

1. Applicants hereby submit the following:
  - [ ] a paper copy of a "Sequence Listing", complying with §1.821(c), to be incorporated into the specification as directed above;
  - [XX] an amendment to the paper copy of the "Sequence Listing" submitted on January 24, 2002, the amendment being in the form of substitute sheets;
  - [XX] the Sequence Listing in computer readable form, complying with §1.821(e) and §1.824, including, if an amendment to the paper copy is submitted, all previously submitted data with the amendment incorporated therein;
  - [ ] a substitute computer readable form to replace one found to be damaged or unreadable.
  - [ ] The computer readable form in this application no. 09/... is identical with that filed on .... [date sequence was filed] in application no. 09/ , filed [filing date]. In accordance with 37 C.F.R. §1.821(e), please use the [first-filed, last-filed or only, whichever is applicable] computer readable form filed in that application

as the computer readable form for the instant application. It is understood that the Patent and Trademark Office will make the necessary change in application number and filing date for the instant application. A paper copy of the Sequence Listing is [included in the originally-filed specification of the instant application, included in a separately filed preliminary amendment for incorporation into the specification, whichever is applicable].

[XX] 2. The description has been amended to comply with §1.821(d).

3. The undersigned attorney or agent hereby states as follows:

- (a) this submission is not believed to include new matter [§1.821(g)];
- (b) the contents of the paper copy (as amended, if applicable) and the computer readable form of the Sequence Listing, are believed to be the same [§1.821(f) and §1.825(b)];
- (c) if the paper copy has been amended, the amendment is believed to be supported by the

specification and is not believed to include new matter [§1.825(a)]; and

(d) if the computer readable form submitted herewith is a substitute for a form found upon receipt by the PTO to be damaged or unreadable, that the substitute data is believed to be identical to that originally filed [§1.825(d)].

4. Previous SEQ ID NOS:85 and 86 have been deleted as they were duplicates of SEQ ID NOS:81 and 76, respectively. SEQ ID NOS:85 and 86 in the attached Sequence Listing are now two sequences which were previously not set forth in the Sequence Listing and which are identified on page 86, lines 3-4.

In the sequences appearing at page 180, lines 18-20 of the specification, there are some unusual features. These sequences describe a single partially self-complementary DNA molecule. It contains a noncomplementary hairpin loop indicated by

TTT

| TTT

where the "|" indicates that the leftmost "T" in the top sequence is connected to the leftmost "T" in the bottom sequence. See page 172, lines 20-22.

Thus, SEQ ID NO:87 is the entire strand, whereas SEQ ID NOS:99 and 100 refer to the portions depicted at page 180, line 18 and page 180, line 19, respectively.

There is a similar relationship between SEQ ID NO:88, and SEQ ID NOS:101 and 102 (page 180, lines 30-36); SEQ ID NO:81, and SEQ ID NOS:91 and 92 (page 178, lines 20-23); and SEQ ID NO:82, and SEQ ID NOS:93 and 94 (page 178, lines 30-33).

At the right-hand side of page 180, lines 18-20, there is a poly-(A) tail in the top strand, and hence complementary poly(T) in the bottom strand. The "..." at the end of page 180, line 19, indicates that the tail continues, see page 172, line 20. Hence, the additional "TTTTT-" at page 180, line 20, seems extraneously, and we have deleted it, as well as the extraneous "-[1]". thus, on line 21 there is now just a "5'". Also, for consistency's sake, line 18 now ends with "..." instead of "-".

There is also an obvious typographical error in SEQ ID NO:99 on page 180, lines 19-21. The top sequence (SEQ ID NO:99) is 5' to 3', and the bottom sequence is the complementary portion, in 3'-5' order so complementarity can be seen. (The bottom sequence, in 5' to 3' order, is SEQ ID NO:100.) However, there is a discrepancy on the right-hand side of lines 19-20:

AAAAAAA

GTTTTTT

A and G are not complementary. It can be seen from page 180, liens 6-7, that the sequences should have appeared as

CAAAAAAA

GTTTTTT

C and G being complementary.

Hence, sequences 87, 99 and 100 have been corrected.

5. Under U.S. rules, each sequence must be classified in <213> as an "Artificial Sequence", a sequence of "Unknown" origin, or a sequence originating in a particular organism, identified by its scientific name.

Neither the rules nor the MPEP clarify the nature of the relationship which must exist between a listed sequence and an organism for that organism to be identified as the origin of the sequence under <213>.

Hence, counsel may choose to identify a listed sequence as associated with a particular organism even though that sequence does not occur in nature by itself in that organism (it may be, e.g., an epitopic fragment of a naturally occurring protein, or a cDNA of a naturally occurring mRNA, or even a substitution mutant of a naturally occurring sequence). Hence, the identification of an organism in <213> should not

be construed as an admission that the sequence *per se* occurs in nature in said organism.

Similarly, designation of a sequence as "artificial" should not be construed as a representation that the sequence has no association with any organism. For example, a primer or probe may be designated as "artificial" even though it is necessarily complementary to some target sequence, which may occur in nature. Or an "artificial" sequence may be a substitution mutant of a natural sequence, or a chimera of two or more natural sequences, or a cDNA (i.e., intron-free sequence) corresponding to an intron-containing gene, or otherwise a fragment of a natural sequence.

The Examiner should be able to judge the relationship of the enumerated sequences to natural sequences by giving full consideration to the specification, the art cited therein, any further art cited in an IDS, and the results of his or her sequence search against a database containing known natural sequences.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made".

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the specification:

The paragraph beginning at line 1 and ending at line 10 of page 86 has been amended as follows:

N.BstNB I:

5'-GAGTCNNNNN-3' (SEQ ID NO:85)  
3'-CTCAGNNNN-5' (SEQ ID NO:86)

Alw I:

5'-GGATCN>NNNN-3' (SEQ ID NO:103)  
3'-CCTAGNNNNN-5' (SEQ ID NO:104)

The paragraph beginning at line 27 and ending at line 36 of page 86 has been amended as follows:

N.BstNB I:

5'-GAGTCNNNNN-3' (SEQ ID NO:85)  
3'-CTCAGNNNN-5' (SEQ ID NO:86)

Bbv I:

5'-GCAGCNNNNNNNNNNNNNN-3' (SEQ ID NO:105)  
3'-CGTCGN>NNNNNNNNNNNN-5' (SEQ ID NO:106)

The paragraph beginning at line 1 and ending at line 10 of page 87 has been amended as follows:

N.BstNB I:

5'-GAGTCNNNNN-3' (SEQ ID NO:85)  
3'-CTCAGNNNN-5' (SEQ ID NO:86)

Bci VI:

5'-GTATCCNNNNNN-3' (SEQ ID NO:107)  
3'-CATAGGNNNNNN-5' (SEQ ID NO:108)

The paragraph beginning at line 26 and ending at line 35 of page 87 has been amended as follows:

N.BstNB I:

5'-GAGTCNNNNN-3' (SEQ ID NO:85)  
3'-CTCAGNNNN-5' (SEQ ID NO:86)

Bmr I:

5'-ACTGGGNNNNNN-3' (SEQ ID NO:109)  
3'-TGACCCNNNNNN-5' (SEQ ID NO:110)

The paragraph beginning at line 1 and ending at line 10 of page 88 has been amended as follows:

N.BstNB I:

5'-GAGTCNNNNN-3' (SEQ ID NO:85)  
3'-CTCAGNNNN-5' (SEQ ID NO:86)

Bpm I:

5'-CTGGAGNNNNNNNNNNNNNNNNNNNN-3' (SEQ ID NO:111)  
3'-GACCTCNNNNNNNNNNNNNNNN-5' (SEQ ID NO:112)

The paragraph beginning at line 44 and ending at line 45 of page 88 has been amended as follows:

5'-CTGGAGTCNNNNNNNNNNNNNN-3' (SEQ ID NO:113)  
3'-GACCTCAGNNNNNNNNNNNN-5' (SEQ ID NO:114)

The paragraph beginning at line 1 and ending at line 10 of page 89 has been amended as follows:

N.BstNB I:

5'-GAGTCNNNNN-3' (SEQ ID NO:85)  
3'-CTCAGNNNN-5' (SEQ ID NO:86)

Bse RI:

5'-GAGGAGNNNNNNNNNNNN-3' (SEQ ID NO:115)  
3'-CTCCTCAGNNNNNNNNNN-5' (SEQ ID NO:116)

The paragraph beginning at line 30 and ending at line 31 of page 89 has been amended as follows:

5'-GAGGAGTCNNNNNNNN-3' (SEQ ID NO:117)  
3'-CTCCTCAGNNNNNNNN-5' (SEQ ID NO:118)

The paragraph beginning at line 40 and ending at line 49 of page 89 has been amended as follows:

N.BstNB I:

5'-GAGTCNNNN-3' (SEQ ID NO:85)  
3'-CTCAGNNNN-5' (SEQ ID NO:86)

Bsg I:

5'-GTGCAGNNNNNNNNNNNNNNNN-3' (SEQ ID NO:119)  
3'-CACGTCNNNNNNNNNNNNNN-5' (SEQ ID NO:120)

The paragraph beginning at line 38 and ending at line 47 of page 90 has been amended as follows:

N.BstNB I:

5'-GAGTCNNNN-3' (SEQ ID NO:85)  
3'-CTCAGNNNN-5' (SEQ ID NO:86)

Bsm FI:

5'-GGGACNNNNNNNNNNNNNN-3' (SEQ ID NO:121)  
3'-CCCTGNNNNNNNNNNNNN-5' (SEQ ID NO:122)

The paragraph beginning at line 12 and ending at line 21 of page 91 has been amended as follows:

N.BstNB I:

5'-GAGTCNNNN-3' (SEQ ID NO:85)  
3'-CTCAGNNNN-5' (SEQ ID NO:86)

Bsp MI:

5'-ACCTGCNNNNNNNN-3' (SEQ ID NO:123)  
3'-TGGACGNNNNNNNN-5' (SEQ ID NO:124)

The paragraph beginning at line 38 and ending at line 47 of page 91 has been amended as follows:

N.BstNB I:

5'-GAGTCNNNN-3' (SEQ ID NO:85)  
3'-CTCAGNNNN-5' (SEQ ID NO:86)

Eci I:

5'-GGCGGANNNNNNNNNN-3' (SEQ ID NO:125)  
3'-CCGCCTNNNNNNNNNN-5' (SEQ ID NO:126)

The paragraph beginning at line 12 and ending at line 21 of page 92 has been amended as follows:

N.BstNB I:

5'-GAGTCNNNN-3' (SEQ ID NO:85)  
3'-CTCAGNNNN-5' (SEQ ID NO:86)

Fau I:

5'-CCCGCNNNNNNN-3' (SEQ ID NO:127)  
3'-GGCGNNNNNN-5' (SEQ ID NO:128)

The paragraph beginning at line 40 and ending at line 41 of page 92 has been amended as follows:

5'-GAGTCCCGCNNNNNNNN-3' (SEQ ID NO:129)  
3'-CTCAGGGCGNNNNNNNN-5' (SEQ ID NO:130)

The paragraph beginning at line 1 and ending at line 10 of page 93 has been amended as follows:

N.BstNB I:

5'-GAGTCNNNN-3' (SEQ ID NO:85)  
3'-CTCAGNNNN-5' (SEQ ID NO:86)

Fok I:

5'-GGATGN>NNNNNNNNNNNNNN-3' (SEQ ID NO:131)  
3'-CCTACNNNNNNNNNNNNNN-5' (SEQ ID NO:132)

The paragraph beginning at line 27 and ending at line 36 of page 93 has been amended as follows:

N.BstNB I:

5'-GAGTCNNNN-3' (SEQ ID NO:85)  
3'-CTCAGNNNN-5' (SEQ ID NO:86)

Hga I:

5'-GACGCNNNNNNNNNNN-3' (SEQ ID NO:133)  
3'-CTGCGNNNNNNNNNNN-5' (SEQ ID NO:134)

The paragraph beginning at line 1 and ending at line 10 of page 94 has been amended as follows:

N.BstNB I:

5'-GAGTCNNNN-3' (SEQ ID NO:85)  
3'-CTCAGNNNN-5' (SEQ ID NO:86)

Hph I:

5'-GGTGANNNNNNNNN-3' (SEQ ID NO:135)  
3'-CCACTNNNNNNNN-5' (SEQ ID NO:136)

The paragraph beginning at line 27 and ending at line 36 of page 94 has been amended as follows:

N.BstNB I:

5'-GAGTCNNNN-3' (SEQ ID NO:85)  
3'-CTCAGNNNN-5' (SEQ ID NO:86)

Mbo II:

5'-GAAGANNNNNNNNN-3' (SEQ ID NO:137)  
3'-CTTCTNNNNNNNNN-5' (SEQ ID NO:138)

The paragraph beginning at line 1 and ending at line 10 of page 95 has been amended as follows:

N.BstNB I:

5'-GAGTCNNNN-3' (SEQ ID NO:85)  
3'-CTCAGNNNN-5' (SEQ ID NO:86)

Mly I:

5'-GAGTCNNNNN-3' (SEQ ID NO:139)  
3'-CTCAGNNNNN-5' (SEQ ID NO:140)

The paragraph beginning at line 27 and ending at line 36 of page 95 has been amended as follows:

N.BstNB I:

5'-GAGTCNNNN-3' (SEQ ID NO:85)  
3'-CTCAGNNNN-5' (SEQ ID NO:86)

Mnl I:

5'-CCTCBBBBBBB-3' (SEQ ID NO:141)  
3'-GGAGNNNNNNN-5' (SEQ ID NO:142)

The paragraph beginning at line 43 and ending at line 44 of page 95 has been amended as follows:

5'-GAGTCCTCBBBBBBB-3' (SEQ ID NO:143)  
3'-CTCAGGGAGNNNNNNN-5' (SEQ ID NO:144)

The paragraph beginning at line 3 and ending at line 4 of page 96 has been amended as follows:

5'-GAGTCCTCBBBBBBB-3' (SEQ ID NO:145)  
3'-CTCAGGGAGNNNNNNN-5' (SEQ ID NO:146)

The paragraph beginning at line 13 and ending at line 22 of page 96 has been amended as follows:

N.BstNB I:

5'-GAGTCNNNNN-3' (SEQ ID NO:85)  
3'-CTCAGNNNN-5' (SEQ ID NO:86)

Ple I:

5'-GAGTCNNNNNN-3' (SEQ ID NO:139)  
3'-CTCAGNNNNNN-5' (SEQ ID NO:140)

The paragraph beginning at line 39 and ending at line 48 of page 96 has been amended as follows:

N.BstNB I:

5'-GAGTCNNNNN-3' (SEQ ID NO:85)  
3'-CTCAGNNNNN-5' (SEQ ID NO:86)

Sfa NI:

5'-GCATCNNNNNNNNN-3' (SEQ ID NO:147)  
3'-CGTAGNNNNNNNNN-5' (SEQ ID NO:148)

The paragraph beginning at line 18 and ending at line 22 of page 180 has been amended as follows:

TTTT-CGAAACCTTCATTCCAGGGACTTCCTCACTAAGGTTCAAAGGTTCAAACGGATCACAAAAAA-  
| TTT-GCTTGGAAGTAAGGTCCCTGAAAGGAGTGATTCCAAGTTCCAAGTTGCCTAGGTTTTT...

—TTTT-5'-{1

{SEQ ID NO:99, SEQ ID NO:100}

(SEQ ID NO:87, composed of SEQ ID NO:100 (bottom sequence above), 5' to 3',  
and SEQ ID NO:99, top sequence above)